

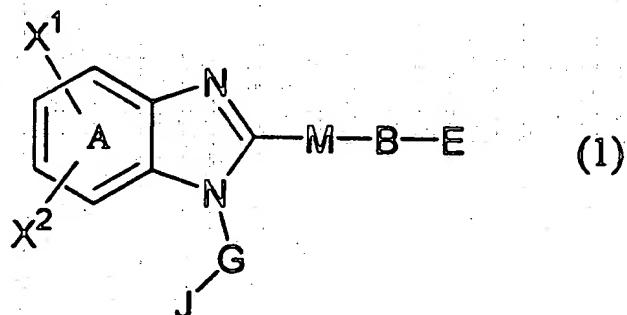
**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

**1-21. (Cancelled)**

**22. (previously presented):** A method of inhibiting human chymase activity to treat or prevent a bone/cartilage metabolic disease in human beings, said method comprising administering to a subject an effective amount of a benzimidazole derivative expressed by the



following formula (1) or its pharmaceutically permissible salt,

[in the formula (1), the ring marked with A expresses a benzene ring;

X<sup>1</sup> and X<sup>2</sup> are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, a cyano group, -CH<sub>2</sub>NH<sub>2</sub>, -CH=NR<sup>1</sup>, -CH=NOR<sup>1</sup> or -CONR<sup>1</sup>R<sup>2</sup> (here, R<sup>1</sup> and R<sup>2</sup> are each a hydrogen atom or a C<sub>1-4</sub> alkyl group), -COOR<sup>3</sup> (here, R<sup>3</sup> is a hydrogen atom or a C<sub>1-4</sub> alkyl group), a substituted or unsubstituted C<sub>1-6</sub> normal, cyclic or branched alkyl group; a substituted or unsubstituted C<sub>3-7</sub> cycloalkyl group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkoxy group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylthio group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched

alkylsulfonyl group or a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylsulfinyl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)};

B is a substituted or unsubstituted C<sub>1-6</sub> normal, cyclic or branched alkylene group or a substituted or unsubstituted C<sub>2-6</sub> normal or branched alkenylene group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C<sub>1-6</sub> normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a C<sub>1-6</sub> normal or branched alkylthio group, a C<sub>1-6</sub> normal or branched alkylsulfonyl group, a C<sub>1-6</sub> normal or branched acyl group, a C<sub>1-6</sub> normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s) of the alkylene group or an alkenylene group; between atoms, the alkylene group or alkenylene group optionally contains one or more of -O-, -S-, -SO<sub>2</sub>- or -NR<sup>4-</sup>, but this atom or atomic group does not bond directly to the M, and here R<sup>4</sup> is a hydrogen atom or a C<sub>1-6</sub> normal or branched alkyl group};

E expresses -COOR<sup>4</sup>;

G is a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylene group {between atoms, the alkylene group optionally contains one or more of -O-, -S-, -SO<sub>2</sub>- or -NR<sup>4-</sup>, but this atom or atomic group does not bond directly to the nitrogen atom of the imidazole ring (R<sup>4</sup> is similarly defined as above), and the substituent is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C<sub>1-6</sub> normal or branched alkoxy group (including the case where

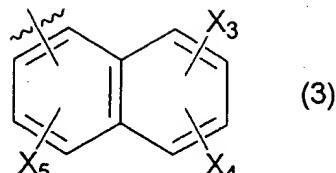
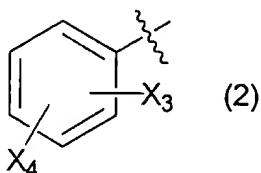
adjacent two groups form an acetal bonding), a trihalomethyl group, a trihalomethoxy group, a phenyl group or an oxo group};

J is a substituted or unsubstituted C<sub>4-10</sub> aryl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, -COOR<sup>7</sup> (here, R<sup>7</sup> is a hydrogen atom or a C<sub>1-4</sub> alkyl group), a C<sub>1-6</sub> normal, cyclic or branched alkyl group, a C<sub>1-6</sub> normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a C<sub>1-6</sub> normal or branched alkylthio group, a C<sub>1-6</sub> normal or branched alkylsulfonyl group, a C<sub>1-6</sub> normal or branched alkylsulfinyl group, a C<sub>1-6</sub> acyl group, a C<sub>1-6</sub> normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group optionally substituted with one or more halogen atoms; the substituent may substitute singly or plurally independently at arbitrary position(s) of the aryl group; and the substituent is further optionally substituted with a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a phenyl group, an oxo group or a phenoxy group optionally substituted with a halogen atom}; and

M is a sulfur atom, a sulfinyl group, or a sulfonyl group].

**23. (previously presented):** The method set forth in Claim 22 wherein X<sup>1</sup> and X<sup>2</sup> in the above formula (1) are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a cyano group, a substituted or unsubstituted C<sub>1-3</sub> normal or branched alkyl group, a substituted or unsubstituted C<sub>1-3</sub> normal or branched alkoxy group, or a substituted or unsubstituted C<sub>1-3</sub> normal or branched alkylthio group.

**24. (previously presented):** The method set forth in Claim 22 wherein J in formula (1) is a group described in the following formula (2) or (3),



[here,  $X^3$ ,  $X^4$  and  $X^5$  are each at the same time or independently a hydrogen atom, a halogen atom, a hydroxyl group, a nitro group, a cyano group, a trihalomethyl group, a trihalomethoxy group,  $-COOR^7$  (here,  $R^7$  is a hydrogen atom or a  $C_{1-4}$  alkyl group), a substituted or unsubstituted  $C_{1-3}$  normal or branched alkyl group, a substituted or unsubstituted  $C_{1-3}$  normal or branched alkoxy group, a substituted or unsubstituted  $C_{1-3}$  normal or branched alkylthio group, a substituted or unsubstituted  $C_{1-3}$  normal or branched alkylsulfonyl group, or a substituted or unsubstituted  $C_{1-3}$  normal or branched alkylsulfinyl group; there is no limitation regarding the substitution positions of  $X^3$ ,  $X^4$  and  $X^5$  on the benzene ring or the naphthalene ring].

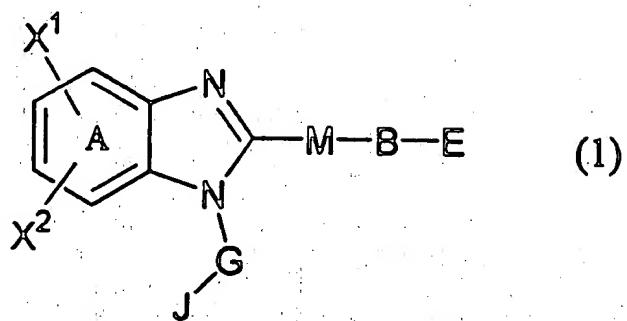
**25. (previously presented):** The method set forth in Claim 22 wherein M is a sulfur atom.

**26. (previously presented):** The method set forth in Claim 22 wherein B is a substituted or unsubstituted C<sub>1-6</sub> normal, cyclic or branched alkylene group.

**27. (currently amended):** The method set forth in Claim 22 wherein G is -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CO-, -CH<sub>2</sub>CH<sub>2</sub>O-, -CH<sub>2</sub>CONH-, -CO-, -SO<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, -CH<sub>2</sub>S- or -CH<sub>2</sub>CH<sub>2</sub>S- (J bonds to the right side of said group).

**28. (previously presented):** The method set forth in Claim 22 wherein E is -COOH.

29. (previously presented): A benzimidazole derivative expressed by the following formula (1) or its pharmaceutically permissible salt,



[in the formula (1), the ring marked with A expresses a benzene ring;

X<sup>1</sup> and X<sup>2</sup> are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, a cyano group, -CH<sub>2</sub>NH<sub>2</sub>, -CH=NR<sup>1</sup>, -CH=NOR<sup>1</sup> or -CONR<sup>1</sup>R<sup>2</sup> (here, R<sup>1</sup> and R<sup>2</sup> are each a hydrogen atom or a C<sub>1-4</sub> alkyl group), -COOR<sup>3</sup> (here, R<sup>3</sup> is a hydrogen atom or a C<sub>1-4</sub> alkyl group), a substituted or unsubstituted C<sub>1-6</sub> normal, cyclic or branched alkyl group, a substituted or unsubstituted C<sub>3-7</sub> cycloalkyl group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkoxy group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylthio group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylsulfonyl group or a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylsulfinyl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)};

B is a substituted or unsubstituted C<sub>1-6</sub> normal, cyclic or branched alkylene group or a substituted or unsubstituted C<sub>2-6</sub> normal or branched alkenylene group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C<sub>1-6</sub> normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a C<sub>1-6</sub> normal or branched alkylthio group, a C<sub>1-6</sub> normal or branched

alkylsulfonyl group, a C<sub>1-6</sub> normal or branched acyl group, a C<sub>1-6</sub> normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s) of the alkylene group or an alkenylene group; between atoms, the alkylene group or alkenylene group optionally contains one or more of -O-, -S- or -SO<sub>2</sub>-, but this atom or atomic group does not bond directly to the M, and here R<sup>4</sup> is a hydrogen atom or a C<sub>1-6</sub> normal or branched alkyl group};

E expresses -COOR<sup>4</sup>;

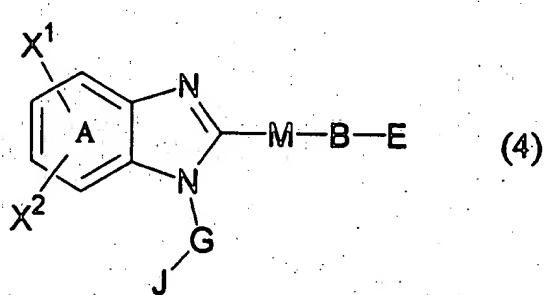
G is a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylene group {between atoms, the alkylene group optionally contains one or more of -O-, -S-, -SO<sub>2</sub>- or -NR<sup>4</sup>-, but this atom or atomic group does not bond directly to the nitrogen atom of the imidazole ring (R<sup>4</sup> is similarly defined as above), and the substituent is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C<sub>1-6</sub> normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a trihalomethyl group, a trihalomethoxy group, a phenyl group or an oxo group};

J is a substituted or unsubstituted C<sub>4-10</sub> aryl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, -COOR<sup>7</sup> (here, R<sup>7</sup> is a hydrogen atom or a C<sub>1-4</sub> alkyl group), a C<sub>1-6</sub> normal, cyclic or branched alkyl group, a C<sub>1-6</sub> normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a C<sub>1-6</sub> normal or branched alkylthio group, a C<sub>1-6</sub> normal or branched alkylsulfonyl group, a C<sub>1-6</sub> normal or branched alkylsulfinyl group, a C<sub>1-6</sub> acyl group, a C<sub>1-6</sub> normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group optionally substituted with one or more halogen atoms; the

substituent may substitute singly or plurally independently at arbitrary position(s) of the aryl group; and the substituent is further optionally substituted with a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a phenyl group, an oxo group or a phenoxy group optionally substituted with a halogen atom}; and  
M is a sulfinyl group, or a sulfonyl group].

**30. (previously presented):** The benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 wherein X<sup>1</sup> and X<sup>2</sup> in the above formula (1) are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a cyano group, a substituted or unsubstituted C<sub>1-3</sub> normal or branched alkyl group, a substituted or unsubstituted C<sub>1-3</sub> normal or branched alkoxy group, or a substituted or unsubstituted C<sub>1-3</sub> normal or branched alkylthio group.

**31. (currently amended):** A benzimidazole derivative expressed by the following formula (4) or its pharmaceutically permissible salt,



[in the formula (4), the ring marked with A expresses a benzene ring;

X<sup>1</sup> and X<sup>2</sup> are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, a cyano group, -CH<sub>2</sub>NH<sub>2</sub>, -CH=NR<sup>1</sup>, -CH=NOR<sup>1</sup> or -CONR<sup>1</sup>R<sup>2</sup> (here, R<sup>1</sup> and R<sup>2</sup> are each a hydrogen atom or a C<sub>1-4</sub> alkyl group), -COOR<sup>3</sup> (here, R<sup>3</sup> is a hydrogen atom or a C<sub>1-4</sub> alkyl group), a substituted or unsubstituted C<sub>1-6</sub>

normal, cyclic or branched alkyl group, a substituted or unsubstituted C<sub>3-7</sub> cycloalkyl group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkoxy group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylthio group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylsulfonyl group or a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylsulfinyl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)};

B is a substituted or unsubstituted C<sub>1-6</sub> normal, cyclic or branched alkylene group or a substituted or unsubstituted C<sub>2-6</sub> normal or branched alkenylene group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C<sub>1-6</sub> normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a C<sub>1-6</sub> normal or branched alkylthio group, a C<sub>1-6</sub> normal or branched alkylsulfonyl group, a C<sub>1-6</sub> normal or branched acyl group, a C<sub>1-6</sub> normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s) of the alkylene group or an alkenylene group; between atoms, the alkylene group or alkenylene group optionally contains one or more of -O-, -S- or -SO<sub>2</sub>-, but this atom or atomic group does not bond directly to the M, and here R<sup>4</sup> is a hydrogen atom or a C<sub>1-6</sub> normal or branched alkyl group};

E expresses -COOR<sup>4</sup>;

G is a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylene group {between atoms, the alkylene group optionally contains one or more of -O-, -S-, -SO<sub>2</sub>- or -NR<sup>4</sup>-, but this

atom or atomic group does not bond directly to the nitrogen atom of the imidazole ring ( $R^4$  is similarly defined as above), and the substituent is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a  $C_{1-6}$  normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a trihalomethyl group, a trihalomethoxy group, a phenyl group or an oxo group};

$J$  is a substituted or unsubstituted  $C_{4-10}$  aryl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group,  $-COOR^7$  (here,  $R^7$  is a hydrogen atom or a  $C_{1-4}$  alkyl group), a  $C_{1-6}$  normal, cyclic or branched alkyl group, a  $C_{1-6}$  normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a  $C_{1-6}$  normal or branched alkylthio group, a  $C_{1-6}$  normal or branched alkylsulfonyl group, a  $C_{1-6}$  normal or branched alkylsulfinyl group, a  $C_{1-6}$  acyl group, a  $C_{1-6}$  normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group optionally substituted with one or more halogen atoms; the substituent may substitute singly or plurally independently at arbitrary position(s) of the aryl group; and the substituent is further optionally substituted with a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a phenyl group, an oxo group or a phenoxy group optionally substituted with a halogen atom}; atom}; and

$M$  is a sulfur atom, a sulfinyl group, or sulfonyl group;

provided that ~~the case is excluded where at least one of when  $X^1$  and  $X^2$  is a~~ are each a group other than a cyano group,  $-CH_2NH_2$ ,  $-CH=NR^1$ ,  $-CH=NOR^1$  or  $-CONR^1R^2$  (here,  $R^1$  and  $R^2$  are each a hydrogen atom or a  $C_{1-4}$  alkyl group), and  $J$  expresses only is a substituted naphthalene ring.

**32. (previously presented):** A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein X<sup>1</sup> and X<sup>2</sup> are each a hydrogen atom, a cyano group, -CH<sub>2</sub>NH<sub>2</sub>, -CH=NR<sup>1</sup>, -CH=NOR<sup>1</sup> or -CONR<sup>1</sup>R<sup>2</sup> (here, R<sup>1</sup> and R<sup>2</sup> are each a hydrogen atom or a C<sub>1-4</sub> alkyl group; X<sup>1</sup> and X<sup>2</sup> are not hydrogen at the same time).

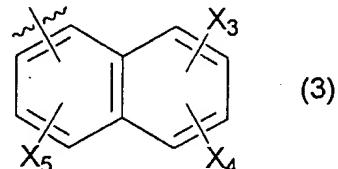
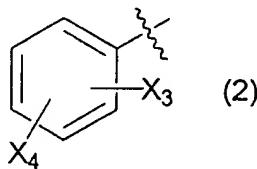
**33. (previously presented):** A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein X<sup>1</sup> and X<sup>2</sup> are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, -COOR<sup>3</sup> (here, R<sup>3</sup> is a hydrogen atom or a C<sub>1-4</sub> alkyl group), a substituted or unsubstituted C<sub>1-6</sub> normal, cyclic or branched alkyl group, a substituted or unsubstituted C<sub>3-7</sub> cycloalkyl, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkoxy group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylthio group, a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylsulfonyl group or a substituted or unsubstituted C<sub>1-6</sub> normal or branched alkylsulfinyl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)}.

**34. (previously presented):** A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein X<sup>1</sup> and X<sup>2</sup> are each a hydrogen atom or a cyano group (here, X<sup>1</sup> and X<sup>2</sup> can not be hydrogen atoms at the same time).

**35. (previously presented):** A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 31 wherein M is a sulfur atom.

**36. (previously presented):** A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein B is a substituted or unsubstituted C<sub>1-6</sub> normal, cyclic or branched alkylene group.

37. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein J is a group expressed by the following formula (2) or (3),



[here,  $X^3$ ,  $X^4$  and  $X^5$  are each at the same time or independently a hydrogen atom, a halogen atom, a hydroxyl group, a nitro group, a cyano group, a trihalomethyl group, a trihalomethoxy group,  $-COOR^7$  (here,  $R^7$  is a hydrogen atom or a  $C_{1-4}$  alkyl group), a substituted or unsubstituted  $C_{1-3}$  normal or branched alkyl group, a substituted or unsubstituted  $C_{1-3}$  normal or branched alkoxy group, a substituted or unsubstituted  $C_{1-3}$  normal or branched alkylthio group, a substituted or unsubstituted  $C_{1-3}$  normal or branched alkylsulfonyl group, or a substituted or unsubstituted  $C_{1-3}$  normal or branched alkylsulfinyl group; there is no limitation regarding the substitution positions of  $X^3$ ,  $X^4$  and  $X^5$  on the benzene ring or the naphthalene ring].

38. (currently amended): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein G is -CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CO-, -CH<sub>2</sub>CH<sub>2</sub>O-, -CH<sub>2</sub>CONH-, -CO-, -SO<sub>2</sub>-, -CH<sub>2</sub>SO<sub>2</sub>-, -CH<sub>2</sub>S- or -CH<sub>2</sub>CH<sub>2</sub>S- (J bonds to the right side of said group).

39. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein E is -COOH.

40. (previously presented): A pharmaceutical composition consisting of a benzimidazole derivative and/or its pharmaceutically permissible salt set forth in any one of Claims 29, 30 or 31, and a pharmaceutically permissible carrier.

41. (currently amended): A method of preventing or treating an inflammatory disease, an allergy disease, a respiratory disease, a cardiovascular disease or a bone/cartilage metabolic disease, said method comprising administering to a subject an effective amount of a A benzimidazole derivative or its pharmaceutically permissible salt set forth in any one of Claims 29, 30 or 31 ~~to prevent or treat an inflammatory disease, an allergy disease, a respiratory disease, a cardiovascular disease or a bone/cartilage metabolic disease.~~

42. (currently amended): A benzimidazole derivative or its pharmaceutically permissible salt The method set forth in Claim 41 to prevent or treat a disease in human beings.